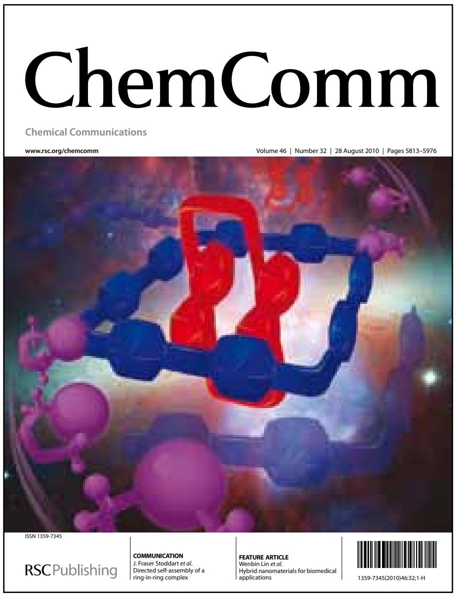
View Online / Journal Homepage

ChemComm

Accepted Manuscript

Downloaded by Indiana University - Purdue University at Indianapolis on 07 October 2012
Published on 05 October 2012 on http://pubs.rsc.org | doi:10.1039/C2CC36196E



ChemComm
Chemical Communications
www.rsc.org/chemcomm
Volume 46 | Number 32 | 28 August 2010 | Pages 5813–5976
ISSN 1359-7345
RSCPublishing
COMMUNICATION
J. Fraser Stoddart *et al.*
Directed self-assembly of a ring-in-ring complex
FEATURE ARTICLE
Wenbin Lin *et al.*
Hybrid nanomaterials for biomedical applications
1359-7345(2010)46:32;1-H

This is an *Accepted Manuscript*, which has been through the RSC Publishing peer review process and has been accepted for publication.

Accepted Manuscripts are published online shortly after acceptance, which is prior to technical editing, formatting and proof reading. This free service from RSC Publishing allows authors to make their results available to the community, in citable form, before publication of the edited article. This *Accepted Manuscript* will be replaced by the edited and formatted *Advance Article* as soon as this is available.

To cite this manuscript please use its permanent Digital Object Identifier (DOI®), which is identical for all formats of publication.

More information about *Accepted Manuscripts* can be found in the **Information for Authors**.

Please note that technical editing may introduce minor changes to the text and/or graphics contained in the manuscript submitted by the author(s) which may alter content, and that the standard **Terms & Conditions** and the **ethical guidelines** that apply to the journal are still applicable. In no event shall the RSC be held responsible for any errors or omissions in these *Accepted Manuscript* manuscripts or any consequences arising from the use of any information contained in them.

RSCPublishing

www.rsc.org/chemcomm
Registered Charity Number 207890

Ruthenium-Catalyzed Oxidative C–H Alkenylation of Aryl Carbamates

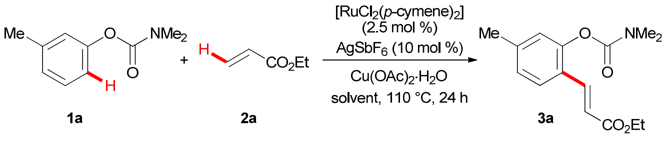
Jie Li, Christoph Kornhaaß and Lutz Ackermann*

Received (in XXX, XXX) Xth XXXXXXXXX 200X, Accepted Xth XXXXXXXXX 200X
First published on the web Xth XXXXXXXXX 200X
DOI: 10.1039/b000000x

A cationic ruthenium(II) catalyst enabled highly efficient oxidative alkenylations of electron-rich arenes bearing removable, weakly coordinating carbamates, and allowed for cross-dehydrogenative C–H bond functionalization in an aerobic manner.

Palladium-catalyzed alkenylations of aryl (pseudo)halides with alkenes, Mizoroki-Heck reactions, have matured to being among the most reliable methods for the synthesis of substituted styrenes.[1, 2] A more atom- and step-economical strategy, however, relies on twofold functionalizations of otherwise unreactive C–H bonds as latent functional groups.[3] The vast majority of these cross-dehydrogenative alkenylations was accomplished using palladium or rhodium complexes, with notable recent progress being accomplished by among others Miura and Yu.[4, 5] On the contrary, less expensive ruthenium complexes were only recently identified as viable catalysts for environmentally benign twofold C–H bond alkenylations. Thereby, carbonyl- and N-heteroaryl-substituted, thus electron-deficient, arenes as well as anilides were converted into the corresponding *ortho*-olefinated[6] products.[7] Contrarily, the use of air- and moisture stable ruthenium complexes for challenging oxidative C–H bond alkenylations with widely accessible phenol derivatives has unfortunately thus far proven elusive. In the course of our continuing efforts in step-economical C–H bond functionalizations,[8] we devised reaction conditions for ruthenium-catalyzed cross-dehydrogenative alkenylations of aryl carbamates bearing removable directing groups, on which we wish to report herein. Importantly, aryl carbamates are key intermediates in organic synthesis, and serve as versatile organic electrophiles in transition-metal-catalysis.[9, 10]
Preliminary studies with a naphthyl carbamate indicated that the desired oxidative alkenylation was not viable with CsOAc or KPF_6 as the co-catalytic additive. However, satisfactory results were gratifyingly achieved when employing 10 mol % of $AgSbF_6$. The desired olefination did not occur in the absence of the ruthenium complex $[RuCl_2(p\text{-cymene})_2]$ (Table 1, entry 1). Among a set of representative solvents, DME turned out to be optimal (entries 2–6), and the catalytic system was found to be air-stable (entry 7). Notably, the cross-dehydrogenative alkenylation failed to proceed in the absence of $AgSbF_6$ as the co-catalyst (entry 8), thus being suggestive of the formation of a cationic ruthenium catalyst. Yet, the preformed cationic complex $[Ru_2Cl_3(p\text{-cymene})_2][PF_6]$[7e] bearing the PF_6-counteranion did not deliver the desired product **3a** under otherwise identical reaction conditions (entry 9).

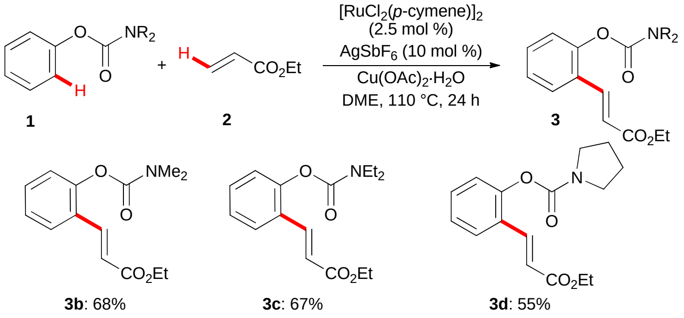
Table 1 Optimization of oxidative alkenylation[a]



Entry	Catalyst	Solvent	Yield (%)
1	---	DME	---
2	$[RuCl_2(p\text{-cymene})_2]$	DMF	---
3	$[RuCl_2(p\text{-cymene})_2]$	PhMe	---
4	$[RuCl_2(p\text{-cymene})_2]$	DCE	40
5	$[RuCl_2(p\text{-cymene})_2]$	*t*-AmOH	48
6	$[RuCl_2(p\text{-cymene})_2]$	DME	84
7	$[RuCl_2(p\text{-cymene})_2]$	DME	86[b]
8	$[RuCl_2(p\text{-cymene})_2]$	DME	---[c]
9	$[Ru_2Cl_3(p\text{-cymene})_2][PF_6]$	DME	---[c]

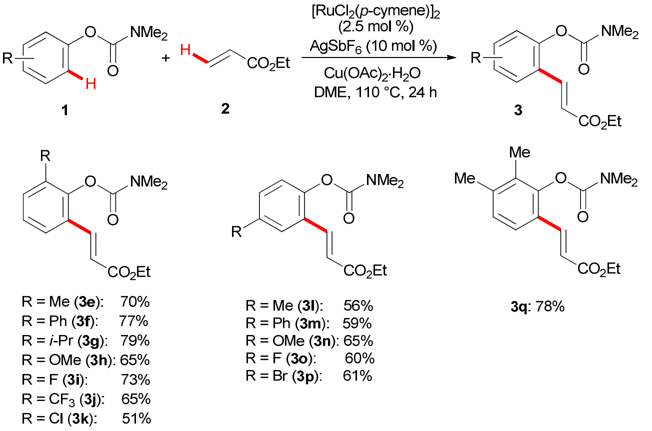
[a] Reaction conditions: **1a** (0.5 mmol), **2a** (1.0 mmol), catalyst (2.5 mol %), $Cu(OAc)_2·H_2O$ (1.0 mmol), solvent (3.0 mL); isolated yields. [b] Under air. [c] Without $AgSbF_6$.

With an optimized catalytic system in hand, we tested the influence of the *N*-substituents of phenyl carbamates **1** on the reaction efficacy (Scheme 1). Thus, dialkyl-substituted carbamates **1** furnished the desired products **3** in high yields, with atom-economical *N*,*N*-dimethyl derivative **1b** providing the best results.



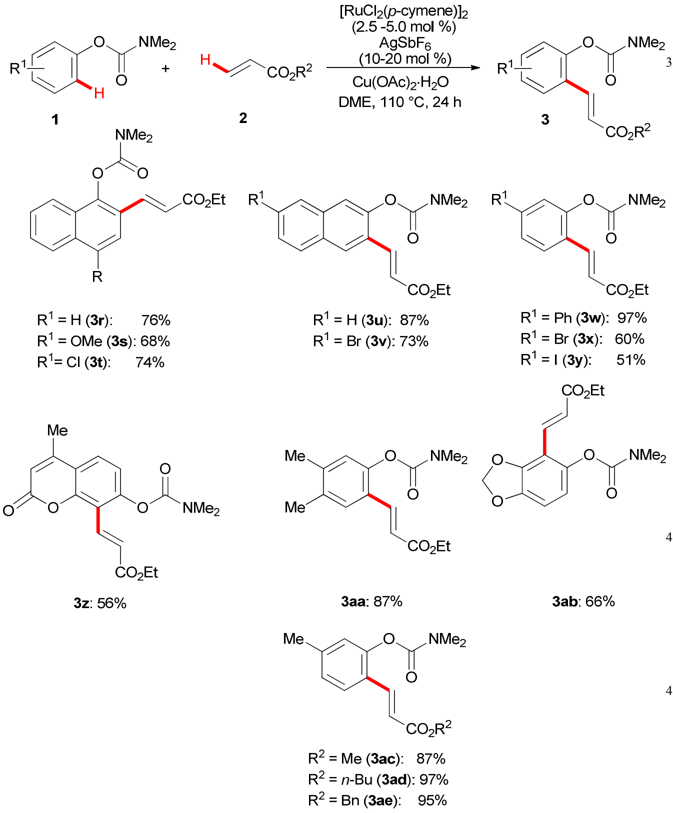
Scheme 1 Effect of *N*-substituents on oxidative C–H bond alkenylation.

Subsequently, we probed the scope of the optimized catalyst in the twofold C–H bond functionalizations with moisture-stable phenol derivatives **1** (Scheme 2). The cationic ruthenium(II) catalyst proved broadly applicable and tolerated valuable functional groups, including aryl and alkyl fluorides, chlorides or bromides, the latter of which should prove valuable for a post-synthetic elaborations of products **3**. Additionally, both electron-deficient as well as electron-rich arenes **1** were found to be suitable substrates, and delivered the corresponding styrenes **3** with excellent *E*-diastereoselectivities.



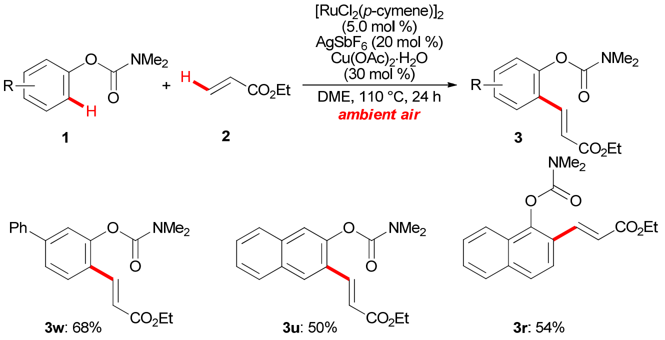
Scheme 2 Scope of oxidative C–H bond alkenylation.

Furthermore, we observed that intramolecular competition experiments with *meta*-substituted substrates **1** proceeded with high site-selectivities, furnishing products **3r**–**3ae** as the sole products (Scheme 3). The ruthenium(II) complex again displayed a useful chemoselectivity, and allowed for the effective conversion of various acrylic esters **2** as well.



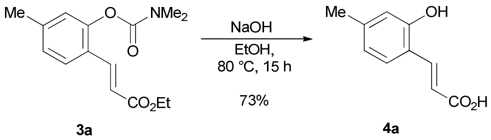
Scheme 3 Scope within intramolecular competition experiments.

Importantly, the double C–H bond functionalization was not limited to the use of stoichiometric amounts of $Cu(OAc)_2{\bullet}H_2O$. Indeed, aerobic oxidative alkenylations proved viable with $Cu(OAc)_2{\bullet}H_2O$ as the cocatalyst under an atmosphere of ambient air (Scheme 4).



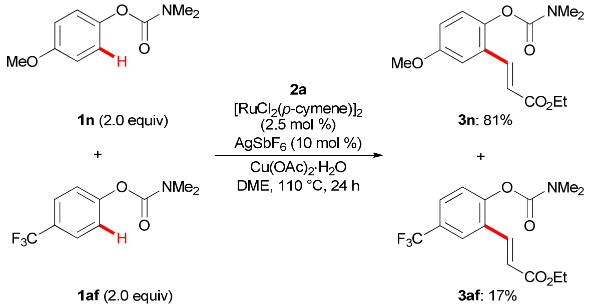
Scheme 4 Aerobic oxidative C–H bond alkenylation.

Importantly, the carbamate directing group was easily removed to deliver the desired phenol **4a** (Scheme 5).



Scheme 5 Removal of directing group.

Considering the remarkable activity and high selectivity of the cationic ruthenium(II) catalyst, we became interested in probing its mode of action. To this end, we conducted intermolecular competition experiments with differently substituted arenes **1**, which revealed electron-rich substrates to be preferentially converted (Scheme 6, and Scheme S-1 in the Supporting Information).



Scheme 6 Intermolecular competition experiments.

Based on these mechanistic studies as well as our previous findings with cationic ruthenium(II) catalysts[7a,e] we propose the catalytic cycle to involve an initial base-assisted, reversible cycloruthenation.[11] Thereafter, coordinative insertion of alkene **2** and β-hydride elimination deliver product **3**, while reductive elimination and reoxidation by $Cu(OAc)_2{\bullet}H_2O$ regenerate the active cationic catalyst.

In conclusion, we have developed ruthenium-catalyzed oxidative C–H bond alkenylations with electron-rich phenol derivatives. Thus, a cationic ruthenium(II) complex set the stage for site-selective, broadly applicable olefinations of aryl carbamates displaying removable directing groups, which also proved viable in an aerobic fashion with ambient air as the ideal terminal oxidant.

Acknowledgements

Financial support by the China Scholarship Council (fellowship to J.L.), and the CaSuS Ph.D. program (fellowship to C.K.) is gratefully acknowledged.

Notes and references

Institut fuer Organische und Biomolekulare Chemie, Georg-August-Universitaet, Tammannstrasse 2, 37077 Goettingen, Germany. Fax:+49 551 396777
E-mail: Lutz.Ackermann@chemie.uni-goettingen.de
Electronic Supplementary Information (ESI) available: See DOI: 10.1039/b000000x/

1. M. Oestreich, *The Mizoroki-Heck Reaction*, Wiley, Weinheim, 2009.
2. M. Beller and C. Bolm, *Transition Metals for Organic Synthesis*, Wiley-VCH, Weinheim, 2004.
3. Selected recent reviews on C−H bond functionalizations: *a*) K. M. Engle, T.-S. Mei, M. Wasa and J.-Q. Yu, *Acc. Chem. Res.*, 2012, **45**, 788; *b*) A. J. Hickman and M. S. Sanford, *Nature*, 2012, **484**, 177; *c*) C. S. Yeung and V. M. Dong, *Chem. Rev.*, 2011, **111**, 1215; *d*) L. McMurray, F. O'Hara and M. J. Gaunt, *Chem. Soc. Rev.*, 2011, **40**, 1885; *e*) J. Wencel-Delord, T. Dröge, F. Liu and F. Glorius, *Chem. Soc. Rev.*, 2011, **40**, 4740; *f*) P. Herrmann and T. Bach, *Chem. Soc. Rev.*, 2011, **40**, 2022; *g*) L. Ackermann and H. K. Potukuchi, *Org. Biomol. Chem.*, 2010, **8**, 4503; *h*) O. Daugulis, *Top. Curr. Chem.*, 2010, **292**, 57; *i*) C.-L. Sun, B.-J. Li and Z.-J. Shi, *Chem. Commun.*, 2010, **46**, 677; *j*) D. A. Colby, R. G. Bergman and J. A. Ellman, *Chem. Rev.*, 2010, **110**, 624; *k*) K. Fagnou, *Top. Curr. Chem.*, 2010, **292**, 35; *l*) M. Livendahl and A. M. Echavarren, *Isr. J. Chem.*, 2010, **50**, 630; *m*) Y. Boutadla, D. L. Davies, S. A. Macgregor and A. I. Poblador-Bahamonde, *Dalton Trans.*, 2009, 5820; *n*) L. Ackermann, R. Vicente and A. Kapdi, *Angew. Chem., Int. Ed.*, 2009, **48**, 9792; *o*) P. Thansandote and M. Lautens, *Chem. Eur. J.*, 2009, **15**, 5874.
4. Selected examples: *a*) R. D. Baxter, D. Sale, K. M. Engle, J.-Q. Yu and D. G Blackmond, *J. Am. Chem. Soc.*, 2012, **134**, 4600; *b*) P. Gandeepan and C.-H. Cheng, *J. Am. Chem. Soc.*, 2012, **134**, 5738; *c*) S. Rakshit, C. Grohmann, T. Besset and F. Glorius, *J. Am. Chem. Soc.*, 2011, **133**, 2350; *d*) M. Ye, G.-L. Gao and J.-Q. Yu, *J. Am. Chem. Soc.*, 2011, **133**, 6964; *e*) S. Mochida, K. Hirano, T. Satoh and M. Miura, *J. Org. Chem.*, 2011, **76**, 3024; *f*) X. Li, X. Gong, M. Zhao, G. Song, J. Deng and X. Li, *Org. Lett.*, 2011, **13**, 5808; *g*) C. Huang, B. Chattopadhyay and V. Gevorgyan, *J. Am. Chem. Soc.*, 2011, **133**, 12406; *h*) Y. Lu, D.-H. Wang, K. M. Engle and J.-Q. Yu, *J. Am. Chem. Soc.*, 2010, **132**, 5916; *i*) D.-H. Wang, K. M. Engle, B.-F. Shi and J.-Q. Yu, *Science*, 2010, **327**, 315; *j*) X. Zhao, C. S. Yeung and V. M. Dong, *J. Am. Chem. Soc.*, 2010, **132**, 5837; *k*) R. B. Bedford, R. L. Webster and C. J. Mitchell, *Org. Biomol. Chem.*, 2009, **7**, 4853; *l*) K. Ueura, T. Satoh and M. Miura, *Org. Lett.*, 2007, **9**, 1407; *m*) M. D. K. Boele, G. P. F. van Strijdonck, A. H. M. de Vries, P. C. J. Kamer, J. G. de Vries, and P. W. N. M. van Leeuwen, *J. Am. Chem. Soc.*, 2002, **124**, 1586; *n*) T. Matsumoto and H. Yoshida, *Chem. Lett.*, 2000, **29**, 1064; *o*) M. Miura, T. Tsuda, T. Satoh, S. Pivsa-Art and M. Nomura, *J. Org. Chem.*, 1998, **63**, 5211; *p*) I. Moritani and Y. Fujiwara, *Tetrahedron Lett.*, 1967, **8**, 1119. For rhodium-catalyzed alkenylations of aryl carbamates, see: *q*) T.-J. Gong, B. Xiao, Z.-J. Liu, J. Wan, J. Xu, D.-F. Luo, Y. Fu and L. Liu, *Org. Lett.*, 2011, **13**, 3235; *r*) C. Feng and T.-P. Loh, *Chem. Commun.*, 2011, **47**, 10458.
5. Selected reviews: *a*) G. Song, F. Wang and X. Li, *Chem. Soc. Rev.*, 2012, **41**, 3651; *b*) T. Satoh and M. Miura, *Chem. Eur. J.*, 2010, **16**, 11212; and references cited therein.
6. Examples of related oxidative annulations of alkynes: *a*) L. Ackermann, A. V. Lygin and N. Hofmann, *Angew. Chem., Int. Ed.*, 2011, **50**, 6379; *b*) L. Ackermann, A. V. Lygin and N. Hofmann, *Org. Lett.*, 2011, **13**, 3278; *c*) L. Ackermann, J. Pospech, K. Graczyk and K. Rauch, *Org. Lett.*, 2012, **14**, 930; *d*) L. Ackermann, L. Wang and A. V. Lygin, *Chem. Sci.*, 2012, **3**, 177; *e*) R. K. Chinnagolla and M. Jeganmohan, *Chem. Commun.*, 2012, **48**, 2030; *f*) L. Ackermann and A. V. Lygin, *Org. Lett.*, 2012, **14**, 764; *g*) K. Parthasarathy, N. Senthilkumar, J. Jayakumar and C.-H. Cheng, *Org. Lett.*, 2012, **14**, 3478; *h*) V. S. Thirunavukkarasu, M. Donati and L. Ackermann, *Org. Lett.*, 2012, **14**, 3416, and referencs cited therein.
7. Oxidative alkenylations: *a*) K. Graczyk, W. Ma and L. Ackermann, *Org. Lett.*, 2012, **14**, 4110; *b*) K. Padala, S. Pimparkar, P. Madasamy and M. Jeganmohan, *Chem. Commun.*, 2012, **48**, 7140; *c*) Y. Hashimoto, T. Ortloff, K. Hirano, T. Satoh, C. Bolm and M. Miura, *Chem. Lett.*, 2012, **41**, 151; *d*) B. Li, J. Ma, N. Wang, H. Feng, S. Xu and B. Wang, *Org. Lett.*, 2012, **14**, 736; *e*) L. Ackermann, L. Wang, R. Wolfram and A. V. Lygin, *Org. Lett.*, 2012, **14**, 728; *f*) Y. Hashimoto, T. Ueyama, T. Fukutani, K. Hirano, T. Satoh and M. Miura, *Chem. Lett.*, 2011, **40**, 1165; *g*) P. B. Arockiam, C. Fischmeister, C. Bruneau and P. H. Dixneuf, *Green Chem.*, 2011, **13**, 3075; *h*) L. Ackermann and J. Pospech, *Org. Lett.*, 2011, **13**, 4153; *i*) T. Ueyama, S. Mochida, T. Fukutani, K. Hirano, T. Satoh and M. Miura, *Org. Lett.*, 2011, **13**, 706; *j*) K.-H. Kwon, D. W. Lee and C. S. Yi, *Organometallics*, 2010, **29**, 5748; *k*) H. Weissman, X. Song and D. Milstein, *J. Am. Chem. Soc.*, 2001, **123**, 337.
8. Illustrative reviews: *a*) L. Ackermann, *Pure Appl. Chem.*, 2010, **82**, 1403; *b*) L. Ackermann, *Isr. J. Chem.*, 2010, **50**, 652.
9. C. G. Hartung and V. Snieckus, in *Modern Arene Chemistry* ed. D. Astruc, Wiley-VCH, Weinheim, 2002, pp. 330-367.
10. Reviews on challenging arylations through C–O bond cleavages: *a*) M. Tobisu and N. Chatani, *ChemCatChem*, 2011, **3**, 1410; *b*) B.-J. Li, D-G. Yu, C.-L. Sun and Z.-J. Shi, *Chem. Eur. J.*, 2011, **17**, 1728; *c*) B. M. Rosen, K. W. Quasdorf, D. A. Wilson, N. Zhang, A.-M. Resmerita, N. K. Garg and V. Percec, *Chem. Rev.*, 2011, **111**, 1346. A recent example from our laboratories: *d*) W. Song and L. Ackermann, *Angew. Chem. Int. Ed.*, 2012, **51**, 8251, and references cited therein.
11. *a*) L. Ackermann, *Chem. Rev.*, 2011, **111**, 1315-1345; *b*) D. Lapointe and K. Fagnou, *Chem. Lett.*, 2010, **39**, 1119-1126.